

### **REMARKS**

Claims 1-36, 43 and 45-59 were pending in this application. Claims 1 and 13 have been amended and claim 43 has been canceled without prejudice to Applicant's rights to pursue the subject matter of the canceled claim in one or more related applications. The amendments made herein are for clarification purposes only, and do not narrow the scope of the claims.

Claims 1 and 13 have been amended to clarify that at least one of the donor and target DNA sequences are not the same as each other, such that, upon recombination of the target and donor vectors, a population of variant DNA molecules is generated. Support for this amendment, which is discussed in further detail below, can be found in the specification, for example at page 13, line 30 through page 14, line 11.

No new matter is added. Following entry of the amendments made herein, claims 1-36 and 45-59 will be pending in the instant application.

### **INTERVIEW SUMMARY RECORD**

Applicant and Applicant's representatives thank Examiner Gerald Leffers, Jr. for the courtesy of the recent telephonic interviews in connection with the above-identified application. Pursuant to 37 C.F.R. § 1.133 and M.P.E.P. 713.04, Applicant presents this interview Summary Record of the two interviews of October 21, 2004 between Examiner Gerald Leffers, Jr. and Applicant's representative, Nikolaos C. George, in connection with the above-referenced application.

During the first interview, the outstanding Office Action was discussed. In particular, Applicant's representative, Attorney Nikolaos C. George, discussed with Examiner Leffers, Jr. the proposed amendments to the language of claims 1 and 13. The Examiner indicated that the amendments would be considered when submitted in writing in response to the outstanding Office Action.

During the second interview, Applicant's representative noted to the Examiner that only one of the two two-page PTO Forms 1449 submitted by Applicant in connection with an Information Disclosure Statement on November 21, 2003 had been attached to the Office Action of July 28, 2004. Applicant's representative explained that the Information Disclosure Statement had been submitted in two counterparts with separate express mail numbers, one counterpart accompanying references A01-A47 and B01-B04, and the other accompanying references B05-B21 and C01-C26. The Examiner indicated that he had only received references B05-B21 and C01-C26, and requested that copies of (1) the postcard

stamped by the Patent Office acknowledging receipt of references A01-A47 and B01-B04 and (2) references B01-B04, which are PCT publications, be submitted with this Amendment. The Examiner noted that copies of references A01-A47, which are U.S. patent documents, need not be submitted. Accordingly, Applicant is submitting herewith copies of the postcard stamped by the Patent Office acknowledging receipt of references A01-A47 and B01-B04, references B01-B04, and the appropriate counterpart of the Information Disclosure Statement initially submitted on November 21, 2003, all under express mail number EV 335 858 543 US.

**THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN**

Claims 1-36, 43 and 45-59 stand rejected under 35 U.S.C. § 112, second paragraph, allegedly as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

**The Rejection of Claims 1 and 13**

The Examiner states that claims 1 and 13 are both vague and indefinite in that the end result of the claimed method does not necessarily recapitulate the desired result recited in the preamble of the claim. The Examiner contends that the methods are directed to the generation of a population of variant sequence modules, but there are no steps that clearly relate to the result of producing a population of variant sequence modules.

With respect to the Examiner's statements about the alleged lack of an element directed to a population of sequence variants, without agreeing with the Examiner, and merely to expedite prosecution, Applicant has amended step (a) of claims 1 and 13 to expressly recite that at least one of (1) the first donor DNA sequence and the first target DNA sequence or (2) the second donor DNA sequence and the second target DNA sequence, are not identical to each other.

In conjunction with this amendment to claims 1 and 13, the Examiner's attention is directed to the definition of the term "homologous" on page 13, line 30 through page 14, line 11 of the specification:

As used herein, two sequences are "homologous" if they share a region of sequence identity, optionally interrupted by one or more mis-matched base pairs, such that they are capable of homologous recombinational exchange with each other. In a preferred embodiment, two homologous double-stranded sequences are completely identical. In another embodiment, the extent of homology is interrupted by not more than 1 mismatched base pair every approximately 10 base pairs of identical nucleotides. In a preferred-embodiment, the extent of homology is a continuous stretch of at least 30, 40, 50, 60, 70, 80 90 or 100 base pairs of identical

nucleotides. In various embodiments, the extent of homology between homologous sequences is a continuous stretch of at least 6, 8, 10, 15, 20, 25, 30, 35, 40, 50, 60, 75 or 100 base pairs of identical nucleotides. In an alternative embodiment, a stretch of identical nucleotides can be interrupted by 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 non-identical nucleotides per 100 identical nucleotides. In yet other embodiments, the extent of sequence identity between donor sequences and target sequences (*i.e.*, each pair of first and second sequences) is at least 70%, more preferably at least 75%, more preferably at least 80%, more preferably at least 85%, yet most preferably at least 90% or 95% identity. In certain specific embodiments, the extent of sequence identity between donor and target sequences is at least 92%, 94%, 96%, 98% or 99%. Homologous sequences may be interrupted by one or more non-identical residues, provided they are still efficient substrates for homologous recombination.

Claims 1 and 13, and claims 2-12, 14-36 and 45-59 dependent thereon, as amended herein, require that the first donor DNA sequence be homologous to the first target DNA sequence, and that the second donor DNA sequence be homologous to the second target DNA sequence, but also require that at least one of the donor DNA sequences be different from one of the target DNA sequences, such that the homologous recombination referred to in step (b) of the claims yields a population of DNA variants.

In view of the foregoing amendments and remarks, Applicant submits that the rejection of claims 1 and 13, and claims 2-12, 14-36 and 45-59 dependent thereon under 35 U.S.C. § 112, second paragraph, has been obviated and should be withdrawn.

#### **The Rejection Of Claim 43**

Claim 43 has been rejected under 35 U.S.C. § 112, second paragraph, because this claim is allegedly indefinite.

Without agreeing with this rejection, and merely to expedite prosecution, Applicant has canceled claim 43 without prejudice to Applicant's right to pursue the subject matter of the canceled claim in one or more related applications.

In view of the foregoing, the rejection of claim 43 under 35 U.S.C. § 112, second paragraph is moot and should be withdrawn.

#### **THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, SHOULD BE WITHDRAWN**

Claim 43 has been rejected under 35 U.S.C. § 112, first paragraph, because this claim allegedly lacks written description.

Without agreeing with this rejection, and merely to expedite prosecution, Applicant has canceled claim 43 without prejudice to Applicant's right to pursue the subject matter of the canceled claim in one or more related applications.

In view of the foregoing, the rejection of claim 43 under 35 U.S.C. § 112, first paragraph is moot and should be withdrawn.

**THE REJECTION UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN**

Claim 43 has been rejected under 35 U.S.C. § 102, because this claim is allegedly anticipated by U.S. Patent No. 5,985,598 to Russo et al.

Without agreeing with this rejection, and merely to expedite prosecution, Applicant has canceled claim 43 without prejudice to Applicant's right to pursue the subject matter of the canceled claim in one or more related applications.

In view of the foregoing, the rejection of claim 43 under 35 U.S.C. § 102 is moot and should be withdrawn.

**CONCLUSION**

Applicant respectfully requests that the present amendment and remarks be entered and made of record in the instant application. All pending claims fully meet all statutory requirements for patentability. Withdrawal of the Examiner's rejections and allowance and action for issuance are respectfully requested. Applicant respectfully requests that the Examiner call the undersigned if any questions or issues remain.

Respectfully submitted,

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